*Unlocking the potential of innovative medicines*

# PCI Biotech

## *PCI – An innovative and versatile platform technology for therapeutic enhancement and vaccination*

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*PCI Biotech AS*
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*BIO Investor Forum 2015*
*21 Oct 2015*

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# PCI Biotech at a glance

- A listed cancer-focused biotech company (PCIB, Oslo exchange)
- Market cap ~$10 mill.
- Lean organisation: 10 employees
- Photochemical internalisation (PCI) technology originates from the Norwegian Radium Hospital
  - Continued close collaboration
- Collaboration with ETH and University Hospital Zurich

- Clinical Program
  - Phase I/II with the photosensitiser Amphinex® for the orphan indication inoperable bile duct cancer
- Pre-clinical programs
  - Vaccine delivery technology that provides strongly enhanced T-cell responses
  - Efficient delivery of macromolecules, such as nucleic acid therapeutics

# An experienced management team

## CEO

**Per Walday**

- PhD from the Institute of Biology at University of Oslo
- Previously held the position of Global Head of Project Management at GE Healthcare
- >20 years of senior management experience in pharmaceutical industry; Nycomed, Amersham Health, GE Healthcare
- Experienced in pharmaceutical development, from preclinical research to registration and commercialization of new products
- Extensive international network and thorough understanding of critical success factors in drug development

## CFO

**Ronny Skuggedal**

- MSc Economics and Business Administration from the Norwegian School of Economics (NHH), Master of Professional Accountancy from BI, State Authorised Public Accountant in Norway
- > 10 years experience from auditing and advisory services, serving clients ranging from Norwegian SME to large international and PE structured clients
- Experience from several M&As and exits, and as management for hire in post M&A phase for international company
- Served as Director at PwC prior to joining PCI Biotech

## CSO

**Anders Høgset**

- PhD from the Institute of Biochemistry at the University of Oslo
- > 10 years experience with academic research at the University of Oslo (Medical Faculty) and The Norwegian Radium Hospital
- > 10 years Industrial experience from Nycomed and PCI Biotech, as Senior Scientist, Project Leader, Research Director and CEO (PCI Biotech)
- Co-author on some 60 scientific papers and 9 patents/patent applications.

## CBDO

**Gaël L'Hévéder**

- MSc Bioorganic Chemistry
- >20 years of international pharmaceutical experience in US and EU in major pharmaceutical companies (Aventis, Baxter, Roche), including research, regulatory affairs and >10 years in business development functions including market intelligence and licensing
- Experience in leading clinical-stage licensing transactions on buy side more recently with Roche in Basel, Switzerland as Partnering Director
- Extensive C-level global network

# Scientific Advisors

**Professor Christoph Huber**, Emeritus Professor of Medicine at the Medical School of the Johannes Gutenberg University in Mainz, Germany

**Professor Jan Vermorken,** Emeritus Professor of Oncology at the University of Antwerp, Belgium

**Professor Andrew Hughes,** Strategy Director of the Experimental Cancer Medicine Team at The Christie, Manchester, UK

**Professor Kristian Berg,** Head of Department of Radiation Biology, Institute for Cancer Research, Oslo University Hospital, Norway

# PCI technology – enabling drugs to reach intracellular therapeutic targets

**STEP 1:**

- $TPCS_{2a}$ (S) and the active molecule (D) are injected into the body and carried by the blood stream to the cell

**STEP 2:**

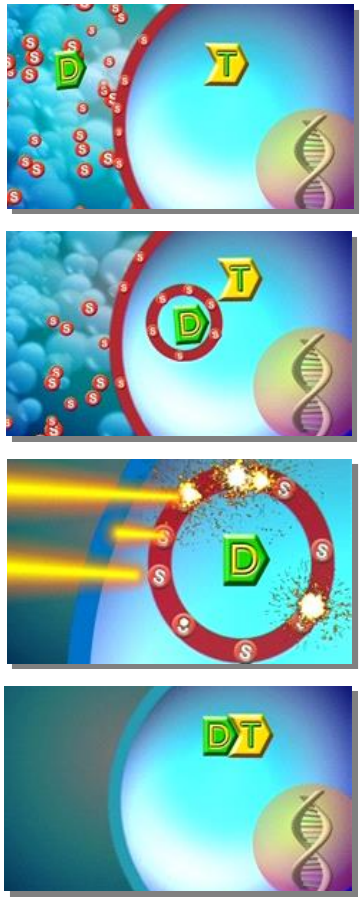
- $TPCS_{2a}$ (S) and the active molecule (D) are taken up by the cell, but D is unable to reach the target (T), as it is encapsulated in an endosome
- S is washed away from the cell membrane, but trapped in endosomes

**STEP 3:**

- Light activates $TPCS_{2a}$ (S) in the membrane of the endosome
- The membrane integrity is affected and the active molecule released

**STEP 4:**

- The active molecule (D) can now bind to its target (T) and initiate the therapeutic response




**The active molecule**
- Anticancer agent, e.g. bleomycin, gemcitabine
- Oligonucleotide, e.g. siRNA
- Protein, e.g. antibody-drug conjugate
- Peptide: e.g. antigen

**The PCI component**
- Light sensitive component
- Amphinex - $TPCS_{2a}$

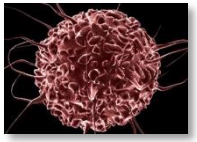
**The target**
- Target for the active molecule
- E.g. DNA, mRNA, enzyme, microtubuli

***PCI mechanism of action – triggered endosomal escape through illumination***

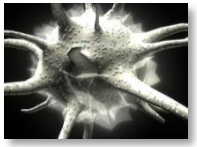
# PCI technology – endosomal escape

## Existing & innovative treatments

### Cells



Cancerous cell



Dendritic cell

### Active ingredient
(trapped in endosome)

- Small molecules
- siRNA/mRNA
- Antibody targeted drugs
- Peptides
- Antigens

## PCI enhancement technology

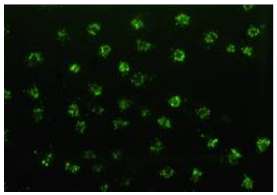
### Photosensitiser
(Fimaporfin)

$TPCS_{2a}$

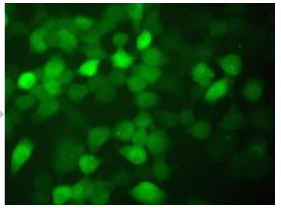
### Light source

Red light

Blue light



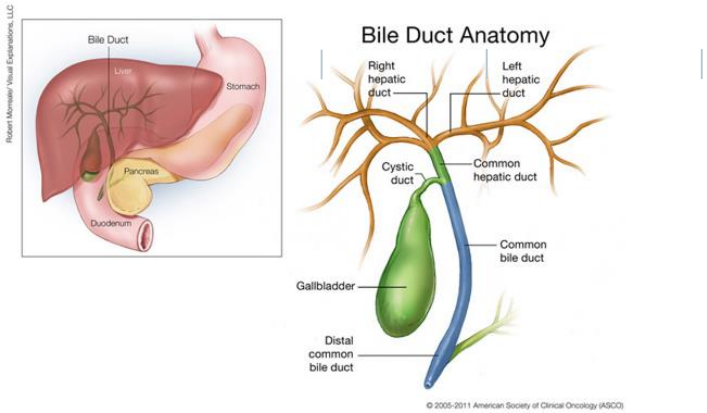
**Endosomal escape**
**Release of drug in cells**



# PCI – a versatile technology with a pipeline of partnering opportunities

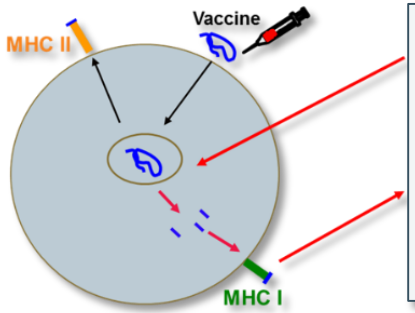
## 1 Local cancer treatment

- Bile duct cancer




## 2 PCI vaccination technology

- Focus on therapeutic vaccination

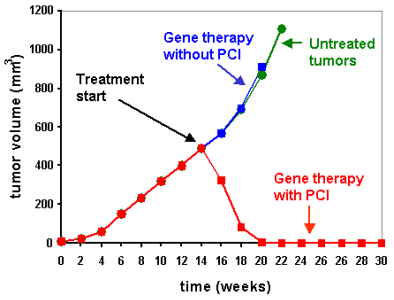



PCI – induce presentation on MHC class I

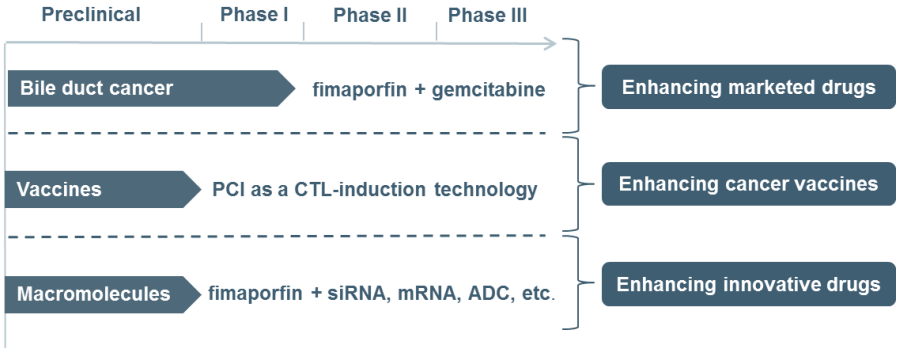
- Make it possible to achieve cytotoxic T-cell response with protein/ peptide vaccines
- Can solve a key challenge for many vaccine approaches

## 3 PCI macromolecule delivery

- siRNA & other oligos
- Gene therapy
- Immunotoxins




## PCI development pipeline



*Amphinex – A New Paradigm for Localised Cancer Treatment*

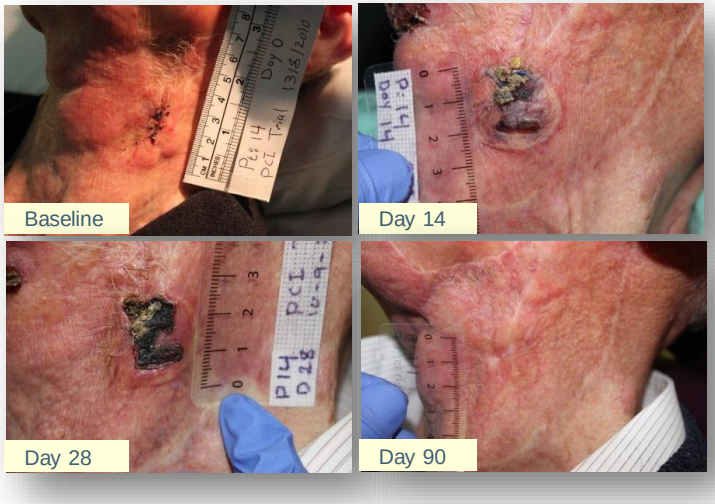
# Amphinex Phase I summary – well tolerated and promising early signs of efficacy

## Summary of design

- Purpose of study was to assess safety and tolerance of Amphinex
- 22 patients with cutaneous and/or subcutaneous tumours
- Surface illumination and Amphinex in combination with bleomycin across 5 dose groups of Amphinex

## Key findings

- Very promising early signs of tumour response across a range of Amphinex dose levels
- Apparent strong selectivity for cancer in several patients
- Well tolerated with appropriate pain control and anaesthesia
- Dose limiting toxicities (“DLT”) at highest dose due to skin photosensitivity and wound infection

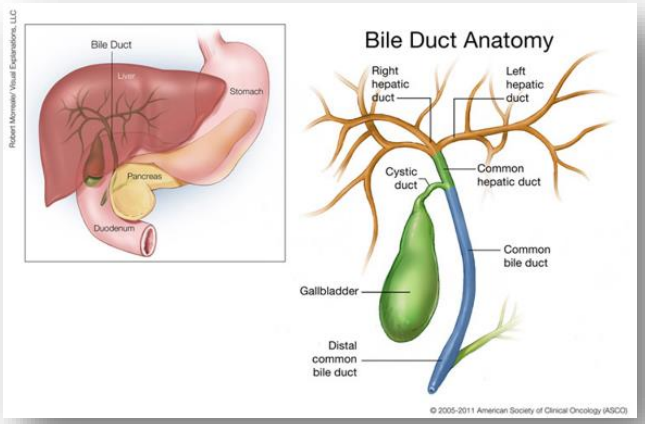



Complete Response following treatment of malignant skin adnexal tumour

# Bile duct cancer – introduction and clinical study design

## Introduction to bile duct cancer

- Cancer affecting the cell lining of the bile duct (Medical term: Cholangiocarcinoma)
- Orphan disease – incidence rate of 1-2 per 100,000 in the western world
- Five-year survival rate of less than 5%, and 0% when inoperable
- Incidence and mortality rates are increasing worldwide




| Summary of Study Design | |
|---|---|
| **Cancer type** | Bile duct (Cholangiocarcinoma) |
| **Phase** | Ib/II |
| **Photosensitizer** | Amphinex® (PCIB) |
| **Drug** | Gemcitabine (Cisplatin) |
| **Light source** | Red laser 652 nm (PCIB) |
| **Fixed variables** | Gemcitabine and Cisplatin |
| **Variables** | Amphinex® and/or light dose |
| **Purpose of study** | Open-label, multi-centre study to assess the safety and efficacy of a single treatment of Amphinex® induced PCI of gemcitabine, followed by systemic cisplatin/ gemcitabine. All patients are stented. Phase I to find light and Amphinex® dose. Phase II randomized to compare PCI vs. stenting alone |
| **Patient description** | Inoperable extrahepatic bile duct cancer |
| **Treatment modality** | Intraluminal illumination |
| **Patient sample size** | Up to 45 patients |
| **Primary endpoint** | Progression free survival |

# Bile duct cancer – an orphan indication with a sizeable market potential

## Immediate target market is as first line treatment

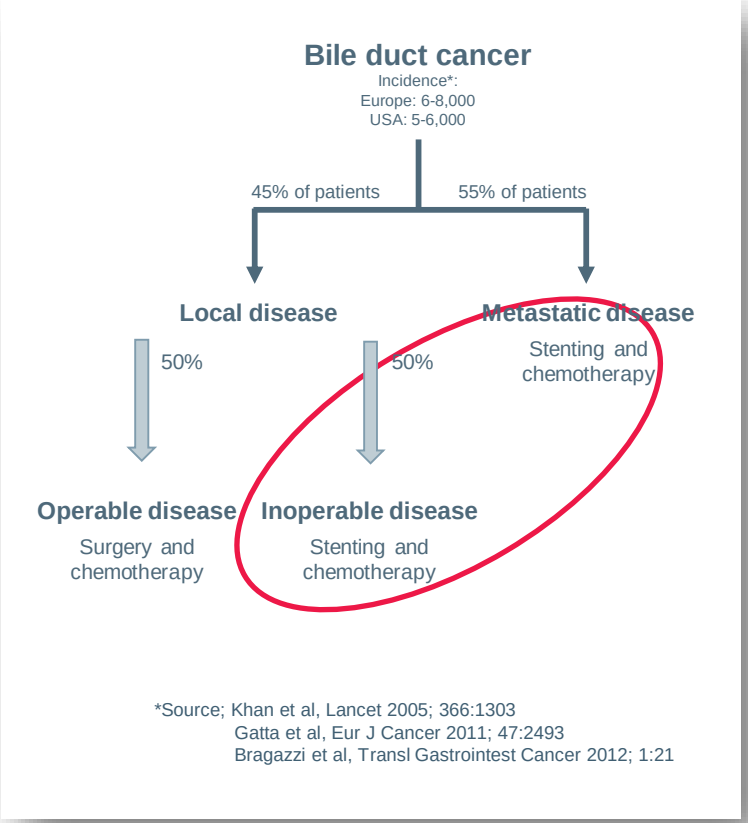
- Target is first-line treatment of inoperable patients
- Approximately 5,000 assumed to be eligible for PCI treatment

## High price potential

- Lack of approved medicinal treatment options
- Orphan indication implies a high price

## Potential significant majority share of the market

- Anticipated benefits
  - ➢ No competing marketable treatment alternatives
  - ➢ Greater efficacy due to local chemotherapy boost
  - ➢ Easy light access through established standard procedures




*Source; Khan et al, Lancet 2005; 366:1303
Gatta et al, Eur J Cancer 2011; 47:2493
Bragazzi et al, Transl Gastrointest Cancer 2012; 1:21

# Clinical study with Amphinex in inoperable bile duct cancer is moving forward

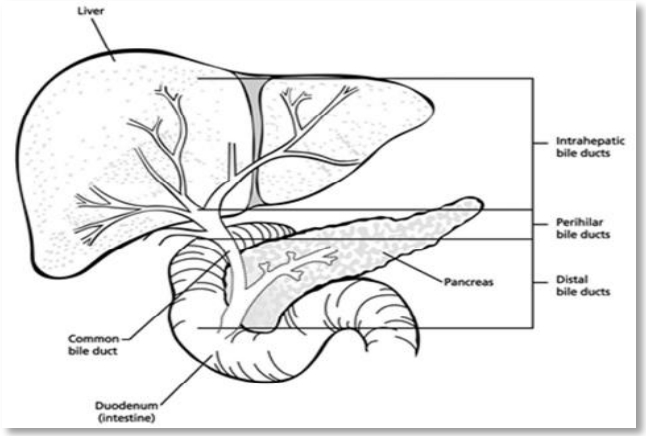
## Why target bile duct cancer?

- **Patient population with high unmet medical need**
- **Orphan indication represents a distinct market opportunity**
- **Easy access with light through routine endoscopic methods**
- **No approved medical treatments**
- **Weak development pipeline**

*Attractive due to orphan benefits and absence of satisfying treatments*

## Current status and plans

- Safety driven Phase Ib
- Third dose cohort concluded Aug 2015 – no safety concerns
- Patient inclusion for the next dose cohort has been initiated
- 5:2 randomisation in Phase II, 35 pts in total
- Increasing the number of sites in preparation for Phase II



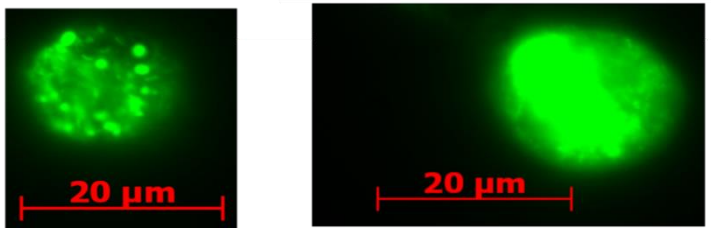
# PCI Biotech

*Unlocking the potential of innovative medicines*

*Unlocking the true potential of new treatment paradigms*

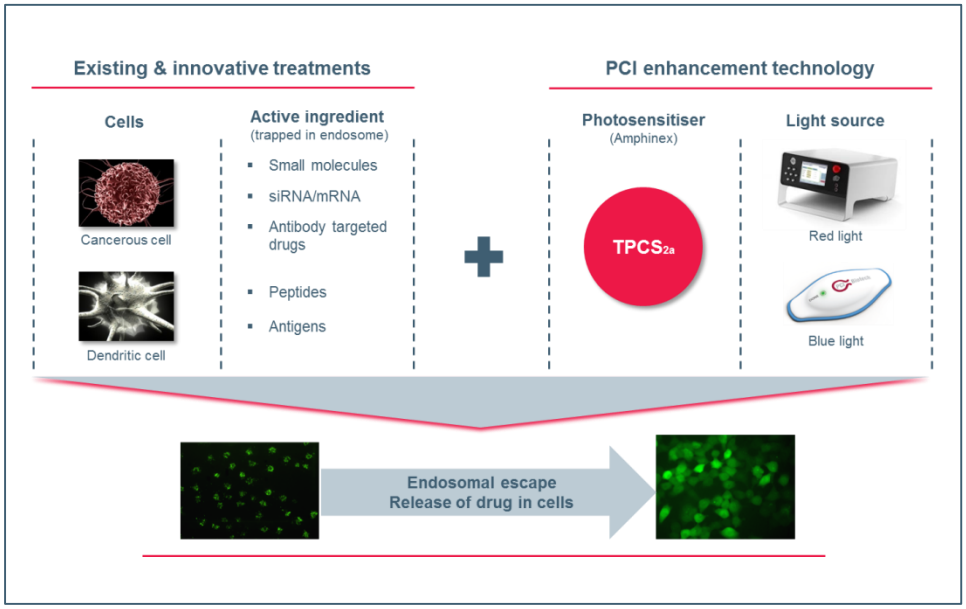
*Immunotherapy*

*Macromolecules*



# Unlocking the true potential of new treatment paradigms

## Enhancement of therapeutic vaccination and delivery of macromolecules

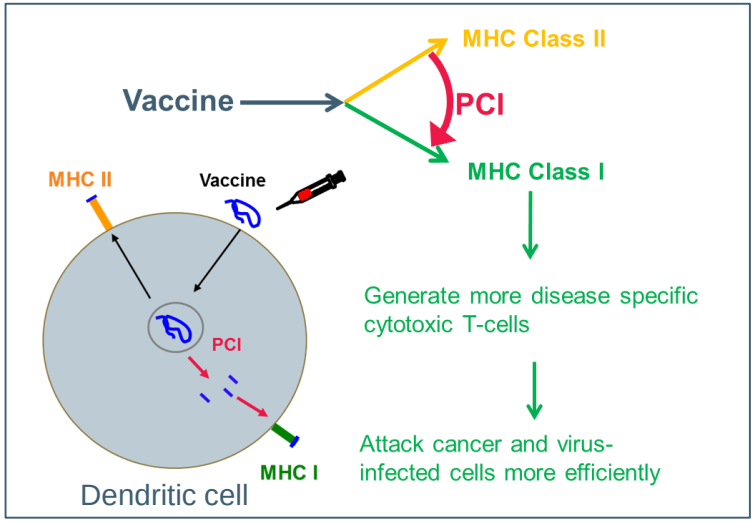



- PCI is a clinically proven endosomal escape technology that may realise the true therapeutic benefit of innovative medicines
- Strong preclinical efficacy evidence
  - ➢ Potentiation of responses considered key for effective **therapeutic vaccination**
  - ➢ Effective localised delivery of a range of **macromolecules**
- Value will be captured through licensing deals and strategic R&D alliances

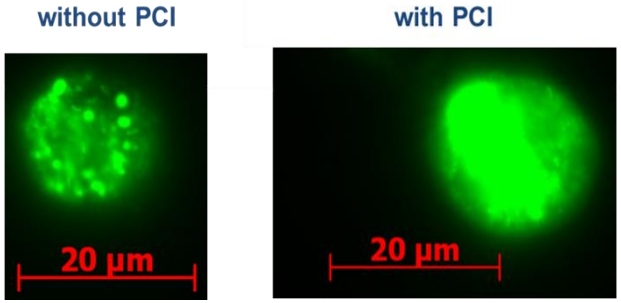
***PCI may realise additional therapeutic potential of innovative medicines and increase their coverage of unmet need in certain disease areas***

# PCI vaccination technology – enhancing vaccine induced cytotoxic T-cell response

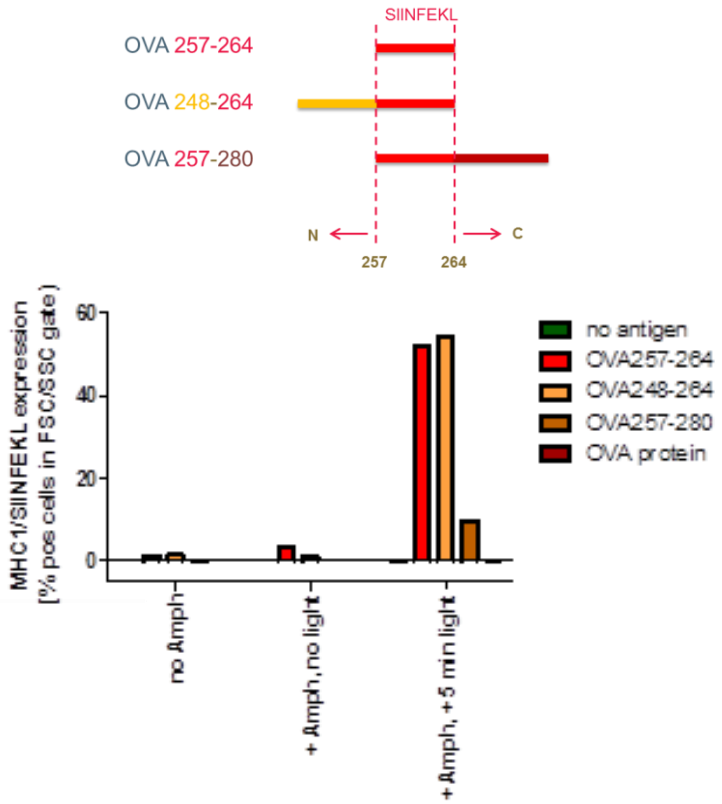
*PCI-induced endosomal antigen escape enhance MHC Class I presentation*




***PCI of OVA-Alexa488 in JAWSII Dendritic cells***

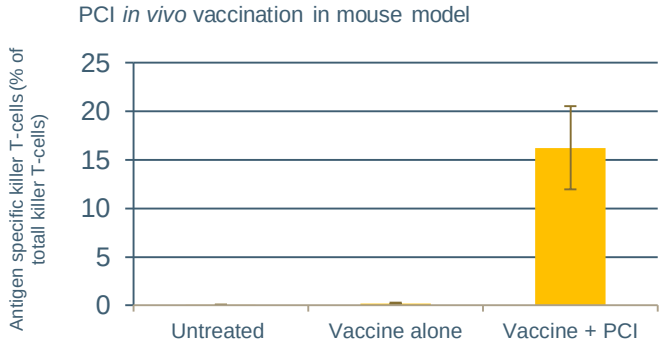



***MHC1/SIINFEKL expression in B6 macrophage***

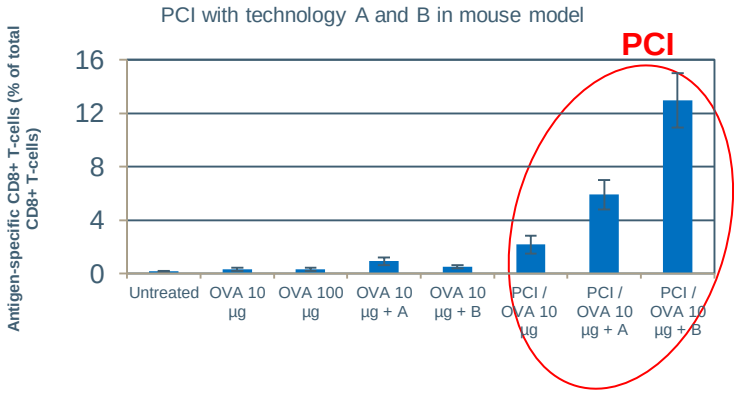


# Therapeutic cancer vaccines – PCI as a powerful CTL-induction technology

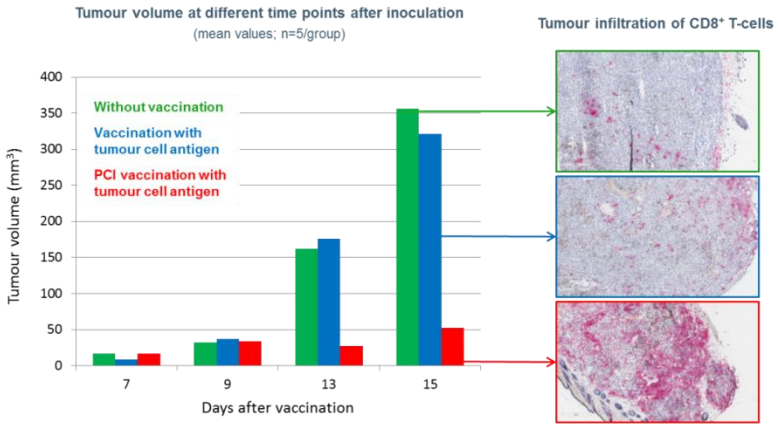
**1** **An effective immune-potentiator,**




**2** **that works in synergy with state-of-the-art vaccine technologies**




**3** **and translates into therapeutic effect in disease models.**



# PCI with HPV peptide antigen – antigen specific CD8 T-cells in blood and tumour regression

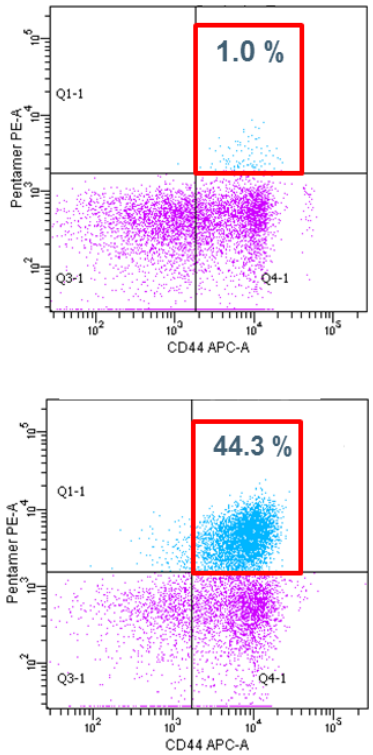
HPV peptide – intradermal vaccination with Poly(IC)

(3 i.d. vaccinations)

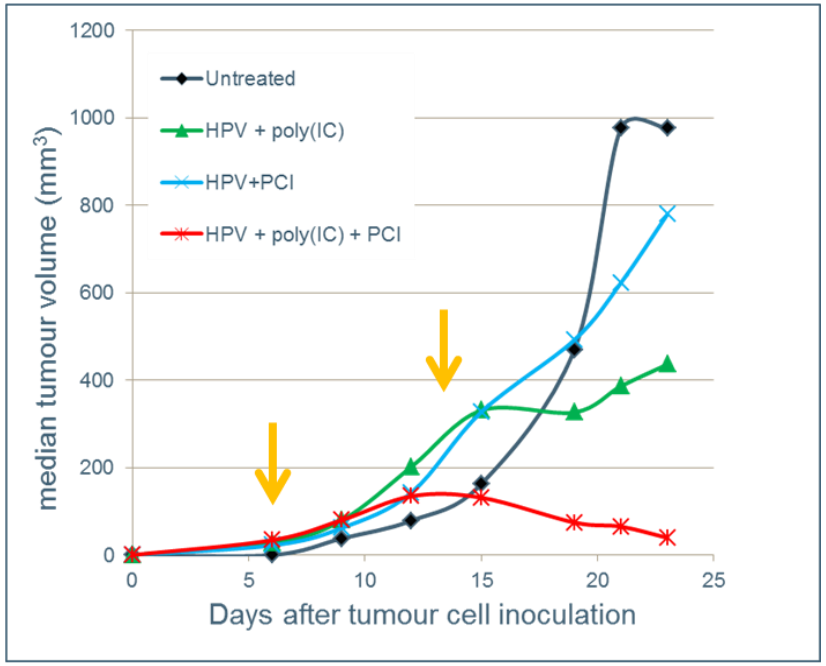
Without PCI:

*Antigen specific CD8 T-cells in blood*

With PCI:




TC-1 mouse tumour model




- Intradermal vaccination at days 6 and 13 after tumour cell inoculation
- 5 animals per group

***Effective CTL-induction with associated tumour regression with a clinically relevant HPV peptide antigen***

# Cancer therapeutic vaccines – competitive advantages and user-friendly PCI solutions

**Safety** – $TPCS_{2a}$ tested in Phase I study (i.v. inj.) at much higher doses than what will be used for vaccination

**Stability** – $TPCS_{2a}$ can be autoclaved and is stable at room temperature, also in solution

**Innovation** – Unique mode of action; indication that $TPCS_{2a}$ provides CTL-induction by MHC class I antigen presentation in dendritic cells and macrophages

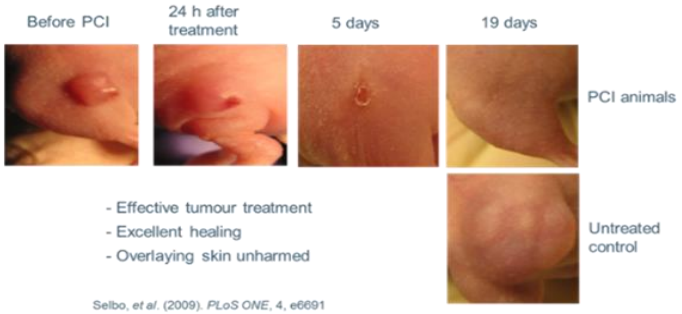

**Cost effectiveness** – Simple and cost effective synthesis of $TPCS_{2a}$

**Broad applicability** – Peptide and protein antigens as well as particulate antigen formulations; Prophylactic & therapeutic vaccination, *in vivo* & *ex vivo*

***Clinical safety and preclinical efficacy evidence, combined with a comprehensive patent estate on PCI-mediated CTL-induction (products, uses and devices)***

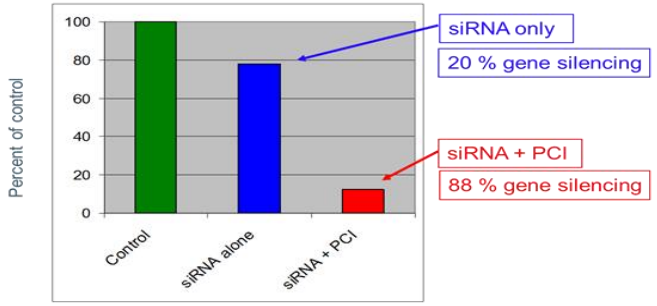
# Macromolecules – endosomal escape of a range of potential partner products

## 1 Intracellular delivery of immunotoxin – *in vivo*



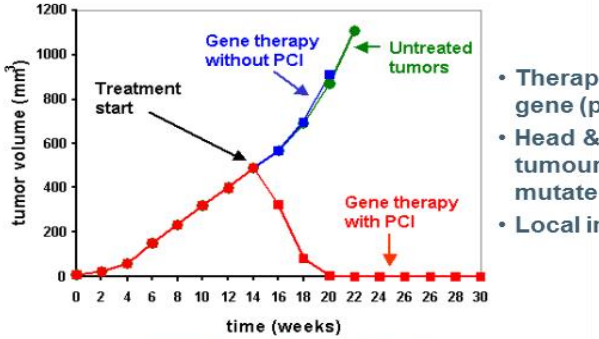

Selbo, *et al.* (2009). *PLoS ONE*, 4, e6691

## 2 Intracellular delivery of siRNA




Bøe, S., Longva, A.S. and Hovig, E. (2007). *Oligonucleotides* 17, 166-73

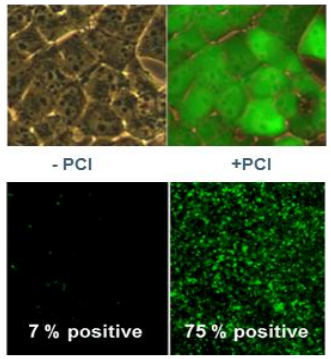
## 3 Intracellular delivery of gene therapy – *in vivo*




- Therapeutic gene (p53)
- Head & neck tumours (p53 mutated)
- Local injection

Ndoye *et al.* (2006) Mol. Ther. **13**:1154-1162

## 4 Intracellular delivery of mRNA




- EGFP mRNA

Bøe, S *et al.* (2010) *Oligonucleotides* **20**:1-6

***Effective intracellular delivery of a range of promising classes of innovative macromolecules***

# Nucleic acid therapeutics – agreement signed with a top-10 large pharma

- **Sept. 2015 – signed pre-clinical agreement with undisclosed top-10 large pharma**
  - **Purpose to determine whether PCI has the potential to enhance the therapeutic effect of their nucleic acid technology platform**
  - **The original evaluation period spans over 9 months**

*"I'm delighted to announce this research agreement with one of the largest pharma companies in the world. We believe that the PCI technology has the potential to play a role in the realisation of several new therapeutic modalities, including cancer immunotherapy and mRNA therapeutics. This agreement shows that external players share this view". Per Walday, CEO.*

## *Financial key elements*

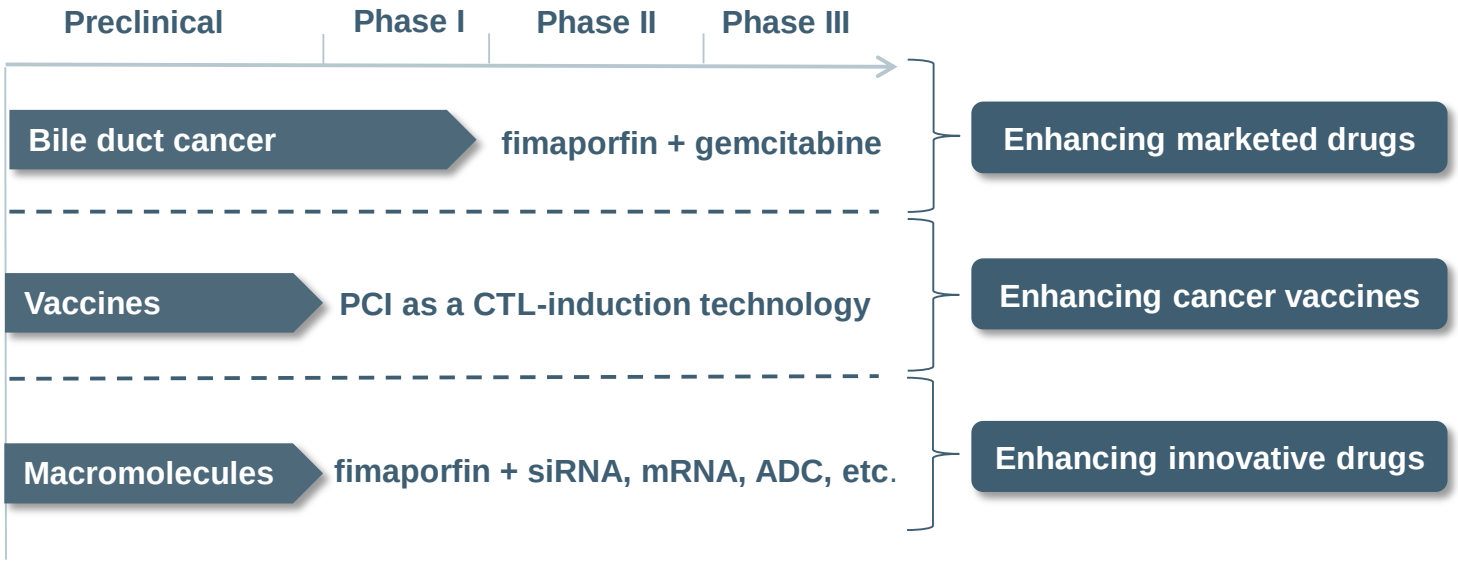
# PCI Biotech

*Financial key elements*

- **Three rounds of financing 2008-2015, totalling to $27 millions**
  - **mainly Norwegian private and institutional investors**
- **Additional $6 million non-dilutive funding**
- **Current market cap $11 million**
- **Financial runway towards end of 2016 at current cost base**

## *Outlook and Strategy*

# PCI Biotech: versatile platform allows for diverse applications in the cancer field



# Development and commercial strategy; Execution plan and future milestones

| | 2015 | 2016 - 2017 |
|---|---|---|
| **Bile duct cancer** | ➢ Progress clinical Phase I dose-escalation part and prepare for initiation of Phase II randomised study | ➢ Orphan drug designation<br>➢ Complete bile duct cancer Phase II study and initiate licensing |
| **Vaccines & Macromolecules** | ➢ Document immune-potentiation in relevant animal models and strengthen products/IP<br>➢ Position PCI in second generation cancer immunotherapy regimen<br>➢ Strategic R&D alliances and licensing | ➢ Strategic collaboration to facilitate further vaccine product development in pre-clinical testing<br>➢ Enter clinical Phase I |

*Focus on research leadership and licensing of the unique proprietary PCI technology*

# Enquiries

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